REMARKS

Claims 1-6, 8-10, 12, 15, 20, and 23-29 are pending in the application. Claims 9, 12, and 20-29 are listed by the Examiner as withdrawn as being drawn to non-elected inventions. Claims 1-6, 8, 10, 11, and 15 are listed as under active consideration. Applicants note that the Examiner appears to have considered claim 12 in this Office Action, and request that the Examiner clarify the status of the claims. Regardless, Applicants have addressed the rejections of claim 12 under 35 U.S.C. 112, first and second paragraphs in this response.

Claims 1, 10, and 15 have been amended and claim 11 has been canceled. To expedite prosecution, claim 1 has been amended to recite that the claimed variants have UDP-glucuronosyltransferase activity, and claim 10 has been amended to recite that the claimed polynucleotide variants encode a polypeptide having UDP-glucuronosyltransferase activity activity. Support for the amendment of claims 1 and 10 can be found in the specification, for example, at Table 2, which identifies the human UDP-glucuronosyltransferase (g3135025) as a homolog of the SEQ ID NO:5 polypeptide and points out the presence of UDP-glucuronosyltransferase motifs in SEQ ID NO:5. By this amendment, Applicants expressly do not disclaim equivalents of the invention which could include polypeptides having biological activities in addition to the recited glucuronosyltransferase activity or polynucleotides encoding such polypeptides. These amendments further clarify the intended subject matter of the claimed invention and address the rejections under 35 U.S.C. § 112, first paragraph. To expedite prosecution, claim 1 has also been amended to recite that the claimed polypeptide variants have at least 95% sequence identity to an amino acid sequence of SEQ ID NO:5 in order to address the rejection under 35 U.S.C. § 102. Support for the amendment of claim 1 can be found in the specification, for example, at page 21, lines 7-10. To expedite prosecution, claim 10 has been amended to recite that the claimed polynucleotide variants have 90% sequence identity to a polynucleotide sequence of SEQ ID NO:10 in order to address the rejection under 35 U.S.C. § 102. Support for the amendment of claim 10 can be found in the specification, for example, at page 21, lines 17-25. Claim 15 has been amended to address the rejection under 35 U.S.C. § 112, second paragraph. These amendments further clarify the intended subject matter of the claimed invention. Entry of these amendments is respectfully requested.

Applicants reserve the right to prosecute non-elected subject matter in subsequent divisional applications.

Comments Regarding Restriction Requirement

Applicants affirm the election with traverse of Group V, which corresponds to claims 1-6, 8, 10, 11, and 15 drawn to polynucleotides, polypeptides, vectors, host cells, and methods of making the polypeptides.

Rejoinder

Applicants reiterate their request that claim 12 (Group IV), which is drawn to a method of using the elected polynucleotides, and claims 20 (Group IX) and 24, which are drawn to methods of using the elected polypeptides, be rejoined per the Commissioner's Notice in the Official Gazette of March 26, 1996, entitled "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)" which sets forth the rules, upon allowance of product claims, for rejoinder of process claims covering the same scope of products. Applicants request that claim 12 (Group IV) be rejoined and examined upon allowance of any of the claims drawn to the polynucleotides of Group V and that claims 20 (Group IX) and 24 be rejoined and examined upon allowance of any of the claims drawn to the polypeptides of Group V.

Objection to the Specification

The Examiner objected to the presence of references to hyperlinks and/or other forms of browser-executable code in the specification (Office Action, page 4). Applicants did not intend to have active links in the specification, nor to incorporate the subject matter of websites by reference to such hyperlinks. Applicants have amended the specification to remove active hyperlinks and therefore respectfully request that the Examiner withdraw the objection to the specification.

Rejection under 35 U.S.C. § 112, second paragraph

Claims 12 and 15 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly being "indefinite for failing to particularly point out and distinctly claim the subject

matter which applicant regards as the invention" (Office Action, page 4). In particular, the Examiner alleges that in claim 12, the phrase "under conditions whereby a hybridizing complex is formed" is indefinite because "[i]t is not clear to the Examiner as to what specific hybridization conditions are contemplated by the applicant." In addition, the Examiner alleges that the term "an effective amount" in claim 15 is indefinite because it is not clear what would be the use of the effective amount of polypeptide. Applicants respectfully traverse the rejection.

Under the second paragraph of 35 U.S.C. § 112, the standard for "definiteness" is that the claims define patentable subject matter with a **reasonable** degree of precision and particularity. See *In re Miller*, 169 USPQ 597, 599 (CCPA 1971); *In re Moore*, 169 USPQ 236, 238 (CCPA 1971). See also MPEP § 706.03(d). In this regard, the Supreme Court has indicated that the primary purpose of claim language is to give "fair" notice of what would constitute the infringement of a claim. See *United Carbon Co. v. Binny & Smith Co.*, 317 U.S. 228, 55 USPQ 381 (1942). In other words, the basic purpose of 35 U.S.C. § 112, second paragraph is to require a claim to reasonably apprise those skilled in the art of the scope of the invention defined by that claim and give fair notice of what constitutes infringement of the claim. See *Antonius v. Pro Group Inc.*, 217 USPQ 875, 877 (6th Cir. 1983). The present claims meet the legal standards required by 35 U.S.C. § 112, second paragraph.

The term "hybridization" is defined in the specification, for example, at page 14, line 25 through page 15, line 26. The "specificity" of hybridization could be ascertained by one of skill in the art by considering the phrase "specifically hybridizes" in the context of claim 12. This claim recites a method of detecting a target polynucleotide, wherein the method relies upon the formation of a specific hybridization complex between a probe polynucleotide and the target polynucleotide. One of skill in the art would understand that the hybridization of the probe and target polynucleotides would require a certain degree of specificity in order to carry out the recited methods of detection. Furthermore, one of skill in the art would **reasonably** conclude that the degree of hybridization specificity is that which is necessary for operability of the recited methods. Therefore, a person of skill in the art would **reasonably** understand the metes and bounds of the phrase "specifically hybridizes" **in the context of the recited methods**.

In order to expedite prosecution, the term "an effective amount" has been removed from claim 15; therefore, the rejection on this basis is moot.

For at least the above reasons, withdrawal of the rejection under 35 U.S.C. § 112, second paragraph is respectfully requested.

Enablement rejections under 35 U.S.C. § 112, first paragraph

Claims 1, 3, 5, 6, 8, 10-12, and 15 are rejected for allegedly failing to meet the requirements of 35 U.S.C. § 112, first paragraph, on the grounds that the Specification does not provide an enabling disclosure commensurate in scope with the claims. In particular, the Examiner alleges that "[i]t would require undue experimentation of the skilled artisan to make and use the claimed polypeptides with an undefined function/activity" (Office Action, page 6). Claims 1 c), 1 d), and 11 have been canceled; therefore, the rejection with respect to these claims is moot. Applicants traverse the rejection for at least the following reasons.

As set forth in *In re Marzocchi*, 169 USPQ 367, 369 (CCPA 1971):

> The first paragraph of § 112 requires nothing more than **objective enablement**. How such a teaching is set forth, either by the use of illustrative examples or by broad terminology, is of no importance.
>
> As a matter of Patent Office practice, then, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented *must* be taken as in compliance with the enabling requirement of the first paragraph of § 112 *unless* there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

Applicants submit that the disclosure amply enables the claimed invention. Given the sequences of SEQ ID NO:5 and SEQ ID NO:10, one of ordinary skill in the art could readily identify a polypeptide comprising a naturally occurring amino acid sequence having at least 95% sequence identity to an amino acid sequence of SEQ ID NO:5, a polynucleotide encoding a polypeptide comprising a naturally occurring amino acid sequence having at least 95% sequence identity to an amino acid sequence of SEQ ID NO:5, and a polynucleotide comprising a naturally occurring polynucleotide sequence having at least 90% sequence identity to a polynucleotide sequence of SEQ ID NO:10, using well known methods of sequence analysis without any undue experimentation. For example, the identification of relevant polynucleotides could be performed

by hybridization and/or PCR techniques that were well-known to those skilled in the art at the time the subject application was filed and/or described throughout the Specification of the instant application. See, e.g., page 14, line 25 through page 15, line 26; page 28, lines 17-28; and Example VI at page 48. Thus, one skilled in the art need not make and test vast numbers of polynucleotides. Instead, one skilled in the art need only screen a cDNA library or use appropriate PCR conditions to identify relevant polynucleotides that already exist in nature. The skilled artisan would also know how to use the claimed polynucleotides, for example in expression profiling, disease diagnosis, or detection of related sequences as discussed above. The specification also describes the expression vectors into which the claimed variants and fragments could be inserted, and the construction of fusion proteins (pages 25-29 and Example IX at pages 49-50).

Applicants respectfully point out that the claims of the instant application are drawn to **naturally occurring** variants. Thus it is not necessary to screen every conceivable variant which might be made using recombinant methods, as all that is claimed are those variant sequences which are found in nature. Through the process of natural selection, nature will have determined the appropriate sequences.

Further, the Examiner requires working examples (Office Action, page 7). There is no such requirement under the law to provide "working examples." As set forth in *In re Borkowski,* 164 USPQ 642, 645 (CCPA 1970) (footnote omitted):

> However, as we have stated in a number of opinions, a specification need not contain a working example if the invention is otherwise disclosed in such a manner that one skilled in the art will be able to practice it without an undue amount of experimentation.

See also M.P.E.P. 2164.02 as follows:

> Compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, does not turn on whether an example is disclosed. An example may be "working" or "prophetic"... A prophetic example describes an embodiment of the invention based on predicted results rather than work actually conducted or results actually achieved.

Thus, there is no requirement under the law to provide "working examples" of what is claimed. Rather, one looks to whether the specification provides a description of how to make what is claimed. The present specification provides the requisite description.

Contrary to the standard set forth in *Marzocchi* and *Borkowski*, the Examiner has failed to provide any ***reasons*** why one would doubt that the guidance provided by the present specification would enable one to make and use the recited polynucleotides and polypeptides. Hence, a *prima facie* case for non-enablement has not been established. For at least the above reasons, withdrawal of the enablement rejections under 35 U.S.C. § 112, first paragraph, is respectfully requested.

Written description rejections under 35 U.S.C. § 112, first paragraph

Claims 1, 3, 5, 6, 8, 10-12, and 15 have been rejected under the first paragraph of 35 U.S.C. 112 for alleged lack of an adequate written description. Claims 1 c), 1 d), and 11 have been canceled; therefore, the rejection with respect to these claims is moot. This rejection is respectfully traversed.

The requirements necessary to fulfill the written description requirement of 35 U.S.C. 112, first paragraph, are well established by case law.

> . . . the applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the "written description" inquiry, *whatever is now claimed. Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991)

Attention is also drawn to the Patent and Trademark Office's own "Guidelines for Examination of Patent Applications Under the 35 U.S.C. Sec. 112, para. 1", published January 5, 2001, which provide that :

> An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail. If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met. (footnotes omitted.)

Thus, the written description standard is fulfilled by both what is specifically disclosed and what is conventional or well known to one skilled in the art.

SEQ ID NO:5 and SEQ ID NO:10 are specifically disclosed in the application (see, for example, page 3, lines 25-28 and page 4, lines 31-32). Variants of SEQ ID NO:5 and SEQ ID NO:10 are described, for example, at page 21, lines 7-10 and lines 17-25. Incyte clones in which the nucleic acids encoding the human UDP-glucuronosyl transferase were first identified and libraries from which those clones were isolated are described, for example, at Tables 1 and 4. Chemical and structural features of SEQ ID NO:5 are described, for example, at Table 2. Given SEQ ID NO:5 and SEQ ID NO:10, one of ordinary skill in the art would recognize a polypeptide comprising a naturally occurring amino acid sequence having at least 95% sequence identity to an amino acid sequence of SEQ ID NO:5, a polynucleotide encoding a polypeptide comprising a naturally occurring amino acid sequence having at least 95% sequence identity to an amino acid sequence of SEQ ID NO:5, and a polynucleotide comprising a naturally occurring polynucleotide sequence having at least 90% sequence identity to a polynucleotide sequence of SEQ ID NO:10. Accordingly, the Specification provides an adequate written description of the recited polypeptide and polynucleotide sequences.

The Office Action has further asserted that the claims are not supported by an adequate written description because "[t]he specification discloses only a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus" (Office Action, page 9).

Such a position is believed to present a misapplication of the law.

1. The present claims specifically define the claimed genus through the recitation of chemical structure

Court cases in which "DNA claims" have been at issue (which are hence relevant to claims to proteins encoded by the DNA) commonly emphasize that the recitation of structural features or chemical or physical properties are important factors to consider in a written description analysis of such claims. For example, in *Fiers v. Revel*, 25 USPQ2d 1601, 1606

(Fed. Cir. 1993), the court stated that:

> If a conception of a DNA requires a precise definition, such as by structure, formula, chemical name or physical properties, as we have held, then a description also requires that degree of specificity.

In a number of instances in which claims to DNA have been found invalid, the courts have noted that the claims attempted to define the claimed DNA in terms of functional characteristics without any reference to structural features. As set forth by the court in *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997):

> In claims to genetic material, however, a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function.

Thus, the mere recitation of functional characteristics of a DNA, without the definition of structural features, has been a common basis by which courts have found invalid claims to DNA. For example, in *Lilly*, 43 USPQ2d at 1407, the court found invalid for violation of the written description requirement the following claim of U.S. Patent No. 4,652,525:

> 1. A recombinant plasmid replicable in procaryotic host containing within its nucleotide sequence a subsequence having the structure of the reverse transcript of an mRNA of a vertebrate, which mRNA encodes insulin.

In *Fiers*, 25 USPQ2d at 1603, the parties were in an interference involving the following count:

> A DNA which consists essentially of a DNA which codes for a human fibroblast interferon-beta polypeptide.

Party Revel in the *Fiers* case argued that its foreign priority application contained an adequate written description of the DNA of the count because that application mentioned a potential method for isolating the DNA. The Revel priority application, however, did not have a description of any particular DNA structure corresponding to the DNA of the count. The court therefore found that the Revel priority application lacked an adequate written description of the subject matter of the count.

Thus, in *Lilly* and *Fiers*, nucleic acids were defined on the basis of functional characteristics and were found not to comply with the written description requirement of 35

U.S.C. §112; *i.e.*, "an mRNA of a vertebrate, which mRNA encodes insulin" in *Lilly*, and "DNA which codes for a human fibroblast interferon-beta polypeptide" in *Fiers*. In contrast to the situation in *Lilly* and *Fiers*, the claims at issue in the present application define polynucleotides or polypeptides in terms of chemical structure, rather than functional characteristics. For example, the "variant language" of independent claims 1 and 10 recite chemical structure to define the claimed genus:

> 1. An isolated polypeptide selected from the group consisting of:...
> b) a polypeptide comprising a naturally occurring amino acid sequence having at least 95% sequence identity to an amino acid sequence of SEQ ID NO:5...
>
> 10. An isolated polynucleotide selected from the group consisting of:...
> b) a polynucleotide comprising a naturally occurring polynucleotide sequence having at least 90% sequence identity to a polynucleotide sequence of SEQ ID NO:10...

From the above it should be apparent that the claims of the subject application are fundamentally different from those found invalid in *Lilly* and *Fiers*. The subject matter of the present claims is defined in terms of the chemical structures of SEQ ID NO:5 or SEQ ID NO:10. In the present case, there is no reliance merely on a description of functional characteristics of the polynucleotides or polypeptides recited by the claims. In fact, there is no recitation of functional characteristics. Moreover, if such functional recitations were included, it would add to the structural characterization of the recited polynucleotides or polypeptides. The polynucleotides or polypeptides defined in the claims of the present application recite structural features, and cases such as *Lilly* and *Fiers* stress that the recitation of structure is an important factor to consider in a written description analysis of claims of this type. By failing to base its written description inquiry "on whatever is now claimed," the Office Action failed to provide an appropriate analysis of the present claims and how they differ from those found not to satisfy the written description requirement in *Lilly* and *Fiers*

2. The present claims do not define a genus which is "highly variant"

Furthermore, the claims at issue do not describe a genus which could be characterized as "highly variant." Available evidence illustrates that the claimed genus is of narrow scope.

In support of this assertion, the Examiner's attention is directed to the enclosed reference by Brenner et al. ("Assessing sequence comparison methods with reliable structurally identified distant evolutionary relationships," Proc. Natl. Acad. Sci. USA (1998) 95:6073-6078). Through exhaustive analysis of a data set of proteins with known structural and functional relationships and with <90% overall sequence identity, Brenner et al. have determined that 30% identity is a reliable threshold for establishing evolutionary homology between two sequences aligned over at least 150 residues. (Brenner et al., pages 6073 and 6076.) Furthermore, local identity is particularly important in this case for assessing the significance of the alignments, as Brenner et al. further report that ≥40% identity over at least 70 residues is reliable in signifying homology between proteins. (Brenner et al., page 6076.)

The present application is directed, *inter alia*, to UDP-glucuronosyl transferases related to the amino acid sequence of SEQ ID NO:5. In accordance with Brenner et al, naturally occurring molecules may exist which could be characterized as UDP-glucuronosyl transferases and which have as little as 40% identity over at least 70 residues to SEQ ID NO:5 or SEQ ID NO:10. The "variant language" of the present claims recites, for example, polynucleotides or polypeptides encoding "a naturally-occurring amino acid sequence having at least 95% sequence identity to the sequence of SEQ ID NO:5 or SEQ ID NO:10" (note that SEQ ID NO:5 has 529 amino acid residues). This variation is far less than that of all potential UDP-glucuronosyl transferase related to SEQ ID NO:5, i.e., those UDP-glucuronosyl transferases having as little as 40% identity over at least 70 residues to SEQ ID NO:5.

3. The state of the art at the time of the present invention is further advanced than at the time of the *Lilly* and *Fiers* applications

In the *Lilly* case, claims of U.S. Patent No. 4,652,525 were found invalid for failing to comply with the written description requirement of 35 U.S.C. §112. The '525 patent claimed the benefit of priority of two applications, Application Serial No. 801,343 filed May 27, 1977, and Application Serial No. 805,023 filed June 9, 1977. In the *Fiers* case, party Revel claimed the benefit of priority of an Israeli application filed on November 21, 1979. Thus, the written

description inquiry in those case was based on the state of the art at essentially at the "dark ages" of recombinant DNA technology.

The present application has a priority date of April 21, 1999. Much has happened in the development of recombinant DNA technology in the 22 or more years from the time of filing of the applications involved in *Lilly* and *Fiers* and the present application. For example, the technique of polymerase chain reaction (PCR) was invented. Highly efficient cloning and DNA sequencing technology has been developed. Large databases of protein and nucleotide sequences have been compiled. Much of the raw material of the human and other genomes has been sequenced. With these remarkable advances one of skill in the art would recognize that, given the sequence information of SEQ ID NO:5 and SEQ ID NO:10, and the additional extensive detail provided by the subject application, the present inventors were in possession of the claimed polynucleotide variants at the time of filing of this application.

4. Summary

The Office Action failed to base its written description inquiry "on whatever is now claimed." Consequently, the Action did not provide an appropriate analysis of the present claims and how they differ from those found not to satisfy the written description requirement in cases such as *Lilly* and *Fiers*. In particular, the claims of the subject application are fundamentally different from those found invalid in *Lilly* and *Fiers*. The subject matter of the present claims is defined in terms of the chemical structure of SEQ ID NO:5 or SEQ ID NO:10. The courts have stressed that structural features are important factors to consider in a written description analysis of claims to nucleic acids and proteins. In addition, the genus of polynucleotides or polypeptides defined by the present claims is adequately described, as evidenced by Brenner et al and consideration of the claims of the '740 patent involved in *Lilly*. Furthermore, there have been remarkable advances in the state of the art since the *Lilly* and *Fiers* cases, and these advances were given no consideration whatsoever in the position set forth by the Office Action.

Rejections under 35 U.S.C. § 102

A. Rejection under 35 U.S.C. § 102(b) in view of Chowdhury et al., Pfeil et al., Makenzie et al., or Jin et al.

Claims 1, 2, and 15 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Chowdhury et al. (1984) Hepatology 4:1074, Pfeil et al. (1983) Eur. J. Biochem. 131:619-624, Mackenzie et al. (1983) J. Steroid Biochem. 19:1097-1102, or Jin et al. (1993) BBRC 194:496-503 on the grounds that the references disclose polypeptides having UDP-glucuronsyl transferase activity. (Applicants note that the claims cannot be rejected under § 102(e) as stated by the Examiner, since none of the cited references are patents.) The Examiner concedes that "the references do not disclose that said polypeptide has the amino acid sequence of SEQ ID NO:5 or that the amino acid sequence of said polypeptides are 90% identical to SEQ ID NO:5." Nevertheless, the Examiner argues that "because the polypeptides have identical activities, Examiner takes the position that a characteristic such as the amino acid sequence is an inherent characteristic of a given polypeptide and therefore the polypeptides of the references have either the same amino acid sequence as that of SEQ ID NO:5 or an amino acid sequence that [sic] at least 90% identical to SEQ ID NO:5" (Office Action, page 10). Applicants disagree and respectfully traverse the rejection.

Applicants respectfully call the Examiner's attention to M.P.E.P. § 706.02 which states that "for anticipation under 35 U.S.C. 102, the reference ***must teach every aspect of the claimed invention either explicitly or impliedly***. Any feature not directly taught must be inherently present" (emphasis added). Furthermore, M.P.E.P. § 2112 states that "[t]he fact that a certain result or characteristic **may** occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic" (emphasis in original). To establish inherency, the extrinsic evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. M.P.E.P. § 2112 further states that "[T]he examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic **necessarily** flows from the teachings of the applied prior art" (emphasis in original). However, the current Office Action provides no such basis or reasoning.

Applicants submit that none of the cited references disclose the polynucleotides and polypeptides of the instant invention, either expressly or inherently. The Examiner's assumption that the sequences of the polypeptides described in the references would "inherently" read on a claim to a polypeptide having the sequence of SEQ ID NO:5 or a variant that is 90% identical is scientifically unsound and clearly wrong. The UDP-glucuronosyltransferases represent an extensive superfamily of enzymes that show individual variability in isozyme substrate specificity and regulation (see enclosed article of Wells et al. (2004) Drug Metab. Disp. 32:281-299). At least 20 distinct UDP-glucuronosyltransferases are known to exist in humans and rats. Wells et al. discuss the importance of identifying and characterizing individual UDP-glucuronosyltransferase enzymes for achieving a better understanding of the role that UDP-glucuronosyltransferase polymorphisms play in cancer susceptibility, drug efficacy, and xenobiotic toxicity.

Although the references cited by the Examiner do not disclose any sequence information, more recently obtained sequence data for glucuronosyltransferases indicate that none of the polypeptides described by the references read on the claims of the instant application. The reference of Jin et al. discloses sequences that are about 80% identical to SEQ ID NO:5 (See recently published sequences of Jin et al. attached at Exhibit A). Applicants note that the references of Chowdhury et al., Pfeil et al., and Makenzie et al. describe rat and mouse liver UDP-glucuronosyltransferase isoforms, not human enzymes such as those described in the instant application. A recent BLAST analysis of SEQ ID NO:5 indicates that rat and mouse liver UDP-glucuronosyltransferases have less than 69% identity with SEQ ID NO:5 (Exhibit B). In particular, Applicants point out that sequences of rat UDP-glucuronosyltransferases described by Mackenzie and Owens are only 66% to 68% identical to SEQ ID NO:5 (Exhibit C) and a mouse UDP-glucuronosyltransferase described by Kimura and Owens is only 66% identical to SEQ ID NO:5 (Exhibit D). Although Chowdhury et al. describe some human isoforms of UDP-glucuronosyltransferase, in view of the large number of human enzymes now known to exist, it would not be clear to one of skill in the art that Chowdhury et al. had isolated an isozyme having the same sequence as SEQ ID NO:5. In fact a search of the GenBank database for all UDP-glucuronosyltransferase sequences currently associated with Chowdhury et al. reveals no polypeptide sequences that are either identical to SEQ ID NO:5, nor variant sequences that are at least 95% identical to SEQ ID NO:5 (Exhibit E).

The Examiner has failed to establish a *prima facie* case for anticipation under 35 U.S.C. 102(b). Therefore, withdrawal of the rejection is respectfully requested.

B. Rejection under 35 U.S.C. § 102(b) in view of Jackson et al.

Claims 1, 3, 5, 6, 8, 10, 11, and 15 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Jackson et al. (1987) Biochem. J. 242:581-588 and Swiss Prot Accession No. P06133 on the grounds that Jackson et al. "disclose the isolation of such a naturally occurring polypeptide having UDP-glucuronosyl transferase activity, and an amino acid sequence that is more than 90% identical to SEQ ID NO:5, a biologically active fragment of the same, an immunogenic fragment of the same, a pharmaceutical composition comprising the same, a polynucleotide encoding the same or that is more than 70% identical to SEQ ID NO:10, vectors and host cells comprising the same and a method of making the encoded polypeptide using said host cells, a polynucleotide comprising at least 60 contiguous nucleotides of said above polynucleotide in a given sample using the method of hybridization" (Office Action, page 11).

Claims 1 c), 1 d), and 11 have been canceled; therefore, the rejection with respect to these claims is moot. Applicants submit that the references of Jackson et al. do not read on claim 1 b), as currently amended, which now recites "a polypeptide comprising a naturally occurring amino acid sequence having at least 95% sequence identity to an amino acid sequence of SEQ ID NO:5," nor claim 10 b), which now recites "a polynucleotide comprising a naturally occurring polynucleotide sequence having at least 90% sequence identity to a polynucleotide sequence of SEQ ID NO:10." Applicants submit that none of the claims, as currently amended, are anticipated by the references of Jackson et al.

For at least these reasons, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 102(b).

C. Rejection under 35 U.S.C. § 102(e) in view of Galvin et al.

Claims 1, 3, 5, 6, 8, 10-12, and 15 are rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Galvin et al. (U.S. Patent No. 6586175, issued 7-1-03 and U.S. 2003/0077629 A1, published 4-24-03) on the grounds that the issued patent and patent application publication "disclose the isolation of such a naturally occurring polypeptide having

UDP-glucuronosyl transferase activity, and an amino acid sequence that is more than 90% identical to SEQ ID NO:5, a biologically active fragment of the same, an immunogenic fragment of the same, a pharmaceutical composition comprising the same, a polynucleotide encoding the same or that is more than 70% identical to SEQ ID NO:10, vectors and host cells comprising the same and a method of making the encoded polypeptide using said host cells, a polynucleotide comprising at least 60 contiguous nucleotides of said above polynucleotide in a given sample using the method of hybridization" (Office Action, page 12).

Claims 1 c), 1 d), and 11 have been canceled; therefore, the rejection with respect to these claims is moot. Applicants submit that the references of Galvin et al. do not read on claim 1 b), as currently amended, which now recites "a polypeptide comprising a naturally occurring amino acid sequence having at least 95% sequence identity to an amino acid sequence of SEQ ID NO:5," nor claim 10 b), as currently amended, which now recites " a polynucleotide comprising a naturally occurring polynucleotide sequence having at least 90% sequence identity to a polynucleotide sequence of SEQ ID NO:10." Applicants submit that none of the claims, as currently amended, are anticipated by the references of Galvin et al.

For at least these reasons, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 102(e).

CONCLUSION

In light of the above amendments and remarks, Applicants submit that the present application is fully in condition for allowance, and request that the Examiner withdraw the outstanding objections/rejections. Early notice to that effect is earnestly solicited.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact the undersigned at the number listed below.

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. 09-0108.

Respectfully submitted,
INCYTE CORPORATION

Date: 26 April 2004

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Enclosures:
Brenner et al. Proc. Natl. Acad. Sci. USA 95:6073-6078 (1998).
Wells et al. Drug Metab. Disp. 32:281-299 (2004).
Exhibit A
Exhibit B
Exhibit C
Exhibit D
Exhibit E